

AMENDMENTS TO THE CLAIMS

This listing of the claims replaces all previous listings.

1. (Canceled)
2. (Currently amended) A method ~~for the treatment or prevention of thrombocythemia in a patient comprising administering to said patient an effective amount of anagrelide or a pharmaceutically acceptable salt of anagrelide in a manner avoiding first pass liver metabolism according to claim 1,~~ wherein anagrelide, ~~the~~ anagrelide in-base form, or a pharmaceutically-acceptable salt of anagrelide ~~salt~~ is administered by means chosen from implants ~~implant~~, sublingual, pregastric absorption, pessary, suppository, transdermal means-nasal, ~~nasal~~ spray, inhaled absorption or topical means ~~administration~~.
3. (Currently amended) A method ~~The method~~ according to claim 1 ~~claim 2~~, wherein anagrelide, ~~the~~ anagrelide in-base form, or a pharmaceutically-acceptable salt of anagrelide ~~salt~~ is administered ~~with a skin permeation enhancer by contacting an area of skin with a skin-permeable form of anagrelide, anagrelide in-base form, or a pharmaceutically acceptable salt of anagrelide.~~
4. (Currently amended) A method ~~The method~~ according to claim 1 ~~claim 2~~, wherein anagrelide, ~~the~~ anagrelide in-base form, or a pharmaceutically-acceptable salt of anagrelide ~~salt~~ is administered to said patient transdermally or subdermally.
5. (Currently amended) A method ~~The method~~ according to claim 4, wherein anagrelide, ~~the~~ anagrelide in-base form, or a pharmaceutically-acceptable salt of anagrelide ~~salt~~ is administered transdermally.
6. (Currently amended) A method ~~The method~~ according to claim 5, wherein anagrelide, ~~the~~ anagrelide in-base form, or a pharmaceutically-acceptable salt of anagrelide ~~salt~~ is in the form of ~~reservoir a reservoir~~ formulation.

7. (Currently amended) ~~A method~~ The method according to claim 5, wherein ~~anagrelide, the anagrelide in base form, or a pharmaceutically acceptable salt of anagrelide salt~~ is in the form of a single layer formulation comprising ~~anagrelide, the anagrelide in base form, or a pharmaceutically acceptable salt of anagrelide salt~~ and at least one adhesive.

8. (Currently amended) ~~A method~~ The method according to claim 5, wherein ~~anagrelide, the anagrelide in base form, or a pharmaceutically acceptable salt of anagrelide salt~~ is in the form of a multiple layer formulation wherein at least one layer of said multiple layer formulation comprises ~~anagrelide, the anagrelide in base form, or a pharmaceutically acceptable salt of anagrelide salt~~ and at least one adhesive.

9. (Currently amended) ~~A method~~ The method according to claim 5, wherein ~~anagrelide, the anagrelide in base form, or a pharmaceutically acceptable salt of anagrelide salt~~ is in the form of a matrix formulation.

10. (Currently amended) ~~A method~~ The method according to claim 4, wherein ~~anagrelide, the anagrelide in base form, or a pharmaceutically acceptable salt of anagrelide salt~~ is administered subdermally.

11. (Currently amended) ~~A method~~ The method according to claim 10, wherein ~~anagrelide, the anagrelide in base form, or a pharmaceutically acceptable salt of anagrelide salt~~ is administered in the form of a matrix implant formulation.

12. (Currently amended) ~~A method~~ The method according to ~~claim 1~~ claim 2, wherein said thrombocythemia is associated with essential thrombocythemia (ET), chronic myelogenous leukemia (CML), polycythemia vera (PV), agnogenic myeloid metaplasia (AMM) or sickle cell anemia(SCA).

13. (Currently amended) ~~A method~~ The method according to ~~claim 1~~ claim 2, wherein ~~anagrelide, the anagrelide in base form, or a pharmaceutically acceptable salt of anagrelide salt~~ is administered in an amount of 0.1 to 20 mg/kg/day.

14. (Currently amended) ~~A method~~ The method according to claim 1 ~~claim 2~~, wherein ~~anagrelide, the anagrelide in base form, or a pharmaceutically acceptable salt of anagrelide salt~~ is administered in a daily dose of 0.5 to 3 mg.

15. (Currently amended) ~~A method~~ The method according to claim 1 ~~claim 2~~, wherein ~~anagrelide, the anagrelide in base form, or a pharmaceutically acceptable salt of anagrelide salt~~ is administered in a daily dose of 1 to 2 mg.

16. (Currently amended) ~~A method~~ The method according to claim 2, wherein ~~anagrelide, the anagrelide in base form, or a pharmaceutically acceptable salt of anagrelide salt~~ is administered topically to the epidermis in the form of an ointment, cream or lotion.

17. (Currently amended) ~~A method~~ The method according to claim 5, wherein ~~anagrelide, the anagrelide in base form, or a pharmaceutically acceptable salt of anagrelide salt~~ is in the form of a composition which further comprises at least one skin permeation enhancer.

18. (Currently amended) ~~A method~~ The method according to claim 17, wherein said at least one ~~penetration~~ skin permeation enhancer is linalool, carvacrol, thymol, citral, menthol or t-anethole.

19. (Currently amended) ~~A method~~ The method according to claim 5, wherein administration is via a transdermal patch having a single-layer drug-in-adhesive system comprising a composition containing ~~anagrelide, the anagrelide in base form, or a pharmaceutically acceptable salt of anagrelide salt, any optional one or more~~ excipients, and at least one skin-contacting adhesive, which is combined with a single backing film.

20. (Currently amended) ~~A method~~ The method according to claim 5, wherein administration is via a transdermal patch having a multi-layer drug-in-adhesive system wherein: (a) said system comprises at least two distinct layers comprising ~~at anagrelide, the anagrelide in base form, or a pharmaceutically acceptable salt of anagrelide salt~~ and at least one adhesive, and a membrane between said at least two layers or (b) said system comprises at least two distinct layers comprising

at ~~anagrelide~~, ~~the anagrelide in-base form~~, or a ~~pharmaceutically-acceptable salt of anagrelide salt~~ and at least one adhesive, and a single backing film.

21. (Currently amended) ~~A method~~ The method according to claim 5, wherein administration is via a transdermal patch having a reservoir transdermal system comprising a liquid compartment containing a solution or suspension of ~~anagrelide~~, ~~the anagrelide in-base form~~, or a ~~pharmaceutically acceptable salt of anagrelide salt~~, a release liner, and between said release liner and said liquid compartment, a semi-permeable membrane and at least one ~~dhesive~~ adhesive.

22. (Currently amended) ~~A method~~ The method according to claim 5, wherein administration is via a transdermal patch having a matrix system comprising a semisolid matrix containing a solution or suspension of ~~anagrelide~~, ~~the anagrelide in-base form~~, or a ~~pharmaceutically-acceptable salt of anagrelide salt~~ which is in direct contact with a release liner, and a skin adhesion component incorporated in an overlay which forms a concentric configuration around said semisolid matrix.

23. (Currently amended) ~~A method~~ The method according to claim 5, wherein administration is via a transdermal patch containing ~~anagrelide~~, ~~the anagrelide in-base form~~, or a ~~pharmaceutically acceptable salt of anagrelide salt~~ intimately distributed in a matrix.

24. (Currently amended) ~~A method~~ The method according to claim 5, wherein administration is via a transdermal patch containing 1 mg to 100 mg of ~~anagrelide~~, ~~the anagrelide in-base form~~, or a ~~pharmaceutically-acceptable salt of anagrelide salt~~ per patch.

25. (Currently amended) ~~A method~~ The method according to claim 5, wherein administration is via a transdermal patch containing an amount of ~~anagrelide~~, ~~the anagrelide in-base form~~, or a ~~pharmaceutically-acceptable salt of anagrelide salt~~ sufficient to provide a daily dose of 0.5 to 3 mg.

26. (Currently amended) ~~A method~~ The method according to claim 5, wherein administration is via a transdermal patch containing a composition comprising ~~anagrelide~~, ~~the anagrelide in-base form~~, or a ~~pharmaceutically-acceptable salt of anagrelide salt~~ and an acrylic adhesive.

27. (Currently amended) ~~A method~~ The method according to claim 26, wherein said composition contains 66 to 99.8% by weight acrylate adhesive.

28. (Currently amended) ~~A method~~ The method according to claim 5, wherein administration is via a transdermal patch containing an amount of ~~anagrelide, the anagrelide in base form, or a pharmaceutically acceptable salt of anagrelide~~ salt, azone, ethanol, water, optionally propylene glycol and Klucel HF.

29. (Currently amended) ~~A method~~ The method according to claim 28, wherein administration is via a transdermal patch containing ~~an amount of anagrelide, the anagrelide in base form, or a pharmaceutically acceptable salt of anagrelide~~ salt, 0.1 to 10 parts by weight azone, from 30 to 69.8 parts ethanol, 29 to 50 parts by weight water, from 0 to 30 parts by weight propylene glycol, and 1 to 5 parts by weight Klucel HF.

30. (Currently amended) ~~A method~~ The method according to claim 5, wherein administration is via a transdermal patch containing ~~anagrelide, the anagrelide in base form, or a pharmaceutically acceptable salt of anagrelide~~ salt, ethanol, and Klucel HF.

31. (Currently amended) ~~A method~~ The method according to claim 30, wherein administration is via a transdermal patch containing ~~an amount of anagrelide, the anagrelide in base form, or a pharmaceutically acceptable salt of anagrelide~~ salt, 85 to 97 parts by weight ethanol and 2 to 14.9 parts Klucel HF.

32. (Currently amended) ~~A method~~ The method according to claim 5, wherein administration is via a transdermal patch ~~containing~~ having an area of 5 cm² to 100 cm².

33. (Currently amended) ~~A method~~ The method according to ~~claim 1~~ claim 2, wherein ~~anagrelide, the anagrelide in base form, or a pharmaceutically acceptable salt of anagrelide~~ salt is administered over a period of time of 1 to 7 days.

34. (Currently amended) ~~A method~~ The method according to ~~claim 1~~ claim 2, wherein ~~anagrelide, the anagrelide in base form, or a pharmaceutically acceptable salt of anagrelide salt~~ is administered over a period of time of 3 to 4 days.

35. (Canceled)

36. (Currently amended) ~~A method~~ The method according to claim 3, wherein said method comprises: (a) contacting said area of skin with ~~a source of skin permeable form of anagrelide, the anagrelide in base form, or a pharmaceutically acceptable salt of anagrelide salt and a skin permeation enhancer~~; and (b) maintaining said source in material transmitting relationship to said area of skin for a period of at least 12 hours.

37. (Currently amended) A method of reducing the platelet count in a patient comprising administering to said patient an effective amount of ~~anagrelide, anagrelide in base form, or a pharmaceutically acceptable salt of anagrelide in a manner whereby~~ avoiding first pass liver metabolism ~~is avoided wherein the anagrelide or anagrelide salt is administered by implant, sublingual, pregastric, pessary, suppository, transdermal, nasal spray, inhaled absorption or topical administration.~~

38. (Currently amended) A method for reducing the side effects associated with the oral administration of anagrelide comprising administering to a patient in need thereof ~~anagrelide, anagrelide in base form, or a pharmaceutically acceptable salt of anagrelide in a manner whereby~~ avoiding first pass liver metabolism ~~is avoided wherein the anagrelide or anagrelide salt is administered by implant, sublingual, pregastric, pessary, suppository, transdermal, nasal spray, inhaled absorption or topical administration.~~

39. (Canceled)

40. (Canceled)

41. (Canceled)

42. (Canceled)

43. (Currently amended) A medical device for the transdermal administration to a patient of anagrelide, anagrelide in base form, or a pharmaceutically acceptable salt of anagrelide, said device comprising: (a) ~~reservoir means~~ a reservoir containing ~~a skin permeable form of anagrelide,~~ anagrelide ~~in base form,~~ or a pharmaceutically acceptable salt of anagrelide and a skin permeation enhancer; (b) ~~an adhesive means for maintaining a said reservoir means in material transmitting relationship to a patient's skin.~~

44. (Canceled)

45. (Currently amended) ~~A device~~ The device according to claim 43, wherein said device is applied to a 5-100 cm² area of skin.

46. (Currently amended) A medical device for transdermal administration to a patient of ~~anagrelide,~~ anagrelide ~~in base form,~~ or a pharmaceutically acceptable salt of anagrelide, comprising, in combination: (a) a reservoir containing ~~a skin permeable form of anagrelide,~~ anagrelide ~~in base form,~~ or a pharmaceutically acceptable salt of anagrelide and a skin permeation enhancer, and said reservoir having a skin proximal, material releasing surface area of 5-100 cm²; and (b) ~~an adhesive in means for maintaining said reservoir in material transmitting relationship to the skin.~~

47. (Canceled)

48. (Canceled)

49. A medical device for transdermal administration to a patient of ~~anagrelide,~~ anagrelide ~~in base form,~~ or a pharmaceutically acceptable salt of anagrelide, comprising: a backing layer, a release liner, and at least one anagrelide composition layer positioned between said backing layer and said release liner, said at least one anagrelide composition layer comprising ~~anagrelide,~~ the anagrelide ~~in base form,~~ or ~~a pharmaceutically acceptable salt of anagrelide salt,~~ and at least one adhesive.